## REMARKS

Reconsideration and allowance of the above-identified application are respectfully requested.

## I. REQUEST FOR INTERVIEW

At the outset, the Applicants would like to request a personal interview in this case once the Examiner has considered the response, and prior to any action being taken on the response (unless the application is allowed). It is respectfully requested that the undersigned be contacted by telephone (703-816-4005) to arrange such an interview.

## II. ADDRESS FOR MAILINGOF FUTURE PAPERS IN THIS MATTER

It is noted that the outstanding action dated November 5, 2001 was mailed to the address of the previous attorneys. This is not understood, since the action prior to the outstanding action, dated September 1, 2000, was mailed to the correct address, namely Nixon & Vanderhye, P.C., 8th Floor, 1100 North Glebe Road, Arlington, VA 22201 (pursuant to the executed Power of Attorney dated February 24, 1998 - copy attached). The Examiner is requested to ensure that the address for mailing all future correspondence in this case is: Nixon & Vanderhye, P.C., 8th Floor, 1100 North Glebe Road, Arlington, VA 22201. Any questions in this regard should be directed to the undersigned. The Examiner is thanked in advance for her help in this matter.

## III. RESPONSE TO REJECTIONS

The claims which the Examiner believes are non-elected i.e. 319, 321, 324-327, 329 and 330 have been cancelled, and claims 320, 322 and 328 were amended in view of the claim cancellations. Claims which the Examiner stated were elected in paper 31 page 2 (or also paper 48 page 2) have been reintroduced:

new claim 331 is the same as old claim 142;

new claim 332 is the same as old claims 164,165,167 and168 combined;

and

new claim 333 is the same as old claim 177.

All claims are directed to a method of treating cancer or a method of reducing the size of a tumor. There are 3 independent claims, 318, 323 and 332. Claims 318 and 323 relate to moderate virulence virus while Claim 332 requires systemic administration for treatment and regression of a tumor.

On page 2 of the Official Action the Examiner cites 35 USC 112, second paragraph and notes that the term "moderate" is a relative term which renders the claim indefinite.

The Examiner's attention is directed to the Peeples Declaration (copy attached for the Examiner's convenience), which relates to the terms "moderate virulence" and "mesogenic" as used in this art. The Examiner's attention is also directed to the Official Action dated July 8, 1997 (paper 31), in which the 35 USC 112 rejections were dropped. The Examiner notes on page 2 of that Official Action:

"The declaration under 37 CFR 1.132 of Mark Peeples is persuasive."

In the declaration, Dr. Peeples notes:

"7. It is my opinion as an expert in NDV, that the above-mentioned patent applications [Ser. Nos. 08/055,519 and 08/260,536] necessarily convey to one of skill in

the art the concept of treating cancer in a mammal with a mesogenic NDV. My opinion is based on the following paragraphs:

8. NDV is categorized in three distinct classes according to its effects on chickens and chicken embryos. "Low virulence" strains are referred to as lentogenic and take 90 to 150 hours to kill chicken embryos at the minimum lethal dose (MLD); "moderate virulence" strains are referred to as mesogenic and take 60 to 90 hours to kill chicken embryos at the MLD; "high virulence" strains are referred to as velogenic and take 40 to 60 hours to kill chicken embryos at the MLD. See Hanson and Brandly, Science, 122:156-157,1955 and Dardiri et al., Am. J. Vet. Res., 918-920, 1961.

9. The patent applications describe NDV as useful to detect and treat cancer in mammals. Since the entire NDV class is comprised of lentogenic, mesogenic and velogenic, the disclosure in the patent application necessarily conveys to one of skill in the art that each of these three categories is inherently included. On this basis alone, I conclude that the patent applications clearly communicate to the skilled worker that mesogenic NDV is employable for treating cancer in mammals.

10. This is particularly strongly the case for mesogenic NDV.

(a) The patent applications specifically exemplify a mesogenic NDV strain to treat cancer. Example 3, page 18 of 08/055,519, and Example 3, page 27 of 08/260,536, describe tumor regression after administration of NDV strain M (Mass-MK107). NDV strain M (Mass-MK107) is well known to be a mesogenic type of Newcastle Disease Virus. See, e.g., Schloer and Hanson, J. Virol., 2:40-47, 1968. Consequently, it would have been necessarily understood by one of skill in the art that

mesogenic strains are specifically included in the methods of treatment described in the patent applications."

Further, support for the phrase "moderate virulence" in claim 318 can be found at page 6 (figure 5 legend).

On page 3 of the Official Action, claims 318, 320, 322, 323, and 328 stand rejected under 35 U.S.C. §112 first paragraph. Reconsideration is requested.

The Examiner notes that the specification does not reasonably enable any person skilled in the art to make and/or use the invention. Again, the Examiner's attention is directed to the Peeples Declaration. Applicants have clearly shown that NDV strains of moderate virulence (mesogenic) have anticancer properties. In the subject specification, there is an example (Example 3, page 27 along with Figure 5) of tumor regression using an NDV strain other than 73-T: the strain MK107. MK107 is a well known mesogenic strain (Hanson and Bradley, Science 1955, 122:156-157 and Schloer and Hanson, J. Virol 1968, 2:40-47). Further support that the disclosure made in the subject application regarding moderate virulence NDV is enabled can be found in commonly owned U.S. Serial No. 09/292,376, where there are examples of antitumor efficacy with two other mesogenic strains of NDV in Examples 21, 22, 23. This is in addition to the extensive examples (Examples 1-10, 16-17, 29 and including an example with human clinical data-Example 20) that used MK107, the known mesogenic strain of NDV.

Intravenous administration is taught in the subject specification. See page 11 second full paragraph " The virus is preferably administered to the mammal by injection (e.g. intravenous....." Further support that the disclosure made in the subject application

regarding intravenous administration is enabled can be found in commonly owned Serial No. 09/292,376, where additional examples are provided of antitumor efficacy using the intravenous route with mesogenic MK107 strain: Examples 3, 9 and 20 (with Example 20 showing clinical human experience of systemic treatment including regressions of 5 tumors).

abn prior to date of this response

The Examiner also notes that "Applicants are also reminded that the broad recitation of "cancer" is not enabled by the specification as originally filed. Again, it appears that fibrosarcoma would be the sole cancer type finding enablement.... Where as here, a claimed genus represents an undefined group of viruses, the required level of disclosure will be greater than, for example, the disclosure of an invention involving a "predictable" factor such as a mechanical or electrical element." 35 USC 112 first paragraph has no requirement that every embodiment of a claim be exemplified. Further, the rejected claims *are* directed to a *defined* group of NDV viruses (see the Peeples Declaration). The claims are enabled as written. The description in the subject specification, the examples therein, as well as subsequent data discussed above, all support that the claims as presented are sufficiently enabled, i.e. the skilled person would know how to make and use NDV for the claimed use.

On page 5 of the Official Action, claims 318, 320, 322, 323, and 328 stand rejected under 35 U.S.C. §112 first paragraph. Reconsideration is requested.

The Examiner notes that "Applicants disclosure fails to provide adequate written description for the invention as broadly claimed." The Examiner also notes that " moderate virulence has not been defined in the specification since the focus of the specification as originally filed is not directed to strains having moderate virulence."

Again, the Examiner's attention is directed to the Peeples Declaration with regard to "moderate virulence" NDV. Further, support for the phrase "moderate virulence" in claim 318 can be found at page 6 (figure 5 legend). The Examiner notes that "the disclosure predominantly provides discussions and examples of NDV 73-T rather than a moderate virulence strain. The written description requirement does not require that what is being claimed be the predominant subject matter of the specification.

The dosages set forth in claim 323 can be found on page 11 of the subject specification.

Claims 318, 320, 322, 323 and 328 stand rejected under: 35 U.S.C. §102(b) as being anticipated by Lorence et al. Reconsideration is requested.

The Examiner is reminded that to make a 35 USC 102 rejection, each limitation of a claim must be taught in the reference cited.

The Examiner notes that "applicant's arguments that examples set forth in pending application Serial No. 09/292,376 provide enablement for that which is instantly claimed is unpersuasive since enablement must be at the time of the invention." The subject application meets the requirements of 35 USC 112 as discussed in detail above. The examples set forth in pending application Serial No. 09/292,376 were noted simply to show that what was stated in the subject application as filed was sufficiently enabled.

The Examiner argues the references cumulatively by contending that "applicant's disclosure fails to define "moderate virulence." Again, the Examiner's attention is directed to the Peeples Declaration which the Examiner found "persuasive" (see above).

Use of a mesogenic strain or a strain of "moderate virulence" (see claims) of NDV is not taught in Lorence et al (1988). Lorence et al (1988) only uses strain 73-T for in

vitro tumor data - there is no in vivo data and no data on dosing and dosages. Strain 73-T used in this 1988 paper for all tumor cell experimentation is a strain of high virulence in contrast to MK107 which is of moderate virulence (see the subject specification, Figure 5 legend on page 6). Nor is *systemic administration* of NDV *in an amount of about 4 x $10^8$ to 4 x $10^{10}$PFU/kg* for treatment of a *tumor*. (Claims 332-333), taught in Lorence et al (1988).

Claims 318, 320, 322, 323 and 328 stand rejected under 35 U.S.C. §102(a) as being anticipated by Reichard et al; and rejected under 35 U.S.C. §102(b) as being anticipated by Reichard et al. Reconsideration is requested.

Reichard et al (1992) as in the Lorence 1988 paper, only use the 73-T strain for studies using tumor cells. Reichard et al (1992) does not teach the use of a strain of "moderate virulence." Nor is *systemic administration* of NDV *in an amount of about 4 x $10^8$ to 4 x $10^{10}$PFU/kg* for treatment of a *tumor* (Claims 332-333), taught in Reichard et al (1992).

Further, in Reichard, mammals with cancer were not treated; instead tumor cells were injected subcutaneously into mice followed immediately by injection of virus into the subcutaneous wheal where the tumor cells were injected. See paragraph bridging pages 449-450 of Reichard et al. This is in contrast to the subject claims for treating cancer in a mammal having cancer.

In addition, the *dose* used in the present application to treat established cancers is at least ten times greater than that used in Reichard et al for the administration of tumor cells and virus (at least 1 x $10^7$ PFU per mouse per injection versus 1 x $10^6$ PFU per mouse per injection in Reichard et al). This dose of 1 x $10^7$ PFU per mouse is

approximately 4 x $10^8$ PFU per kilogram body weight, assuming a 25 gram mouse. This is the dose for intralesional administration of NDV to treat established cancers. For systemic administration, a dose that is 10-fold higher is required. See Example 2 of the subject application. Also, see generally page 13, lines 13-35 and Examples 1-3 and 5 of the subject application. The use of these much higher doses is not taught or suggested by Reichard et al. Indeed, the use of these higher doses is contrary to the teachings of Reichard et al which suggests that only a small number of NDV will be necessary for systemic treatment of tumors (see lines 2-4 from the bottom of the first column on page 452 of Reichard et al).

The viral strains of the subject application are less virulent strains than the 73T strain used in Reichard et al (see Example 3 of the subject application). There is nothing in Reichard et al to teach or suggest that a less virulent strain would be effective in treating cancer.

Should any small matters remain outstanding, Examiner Scheiner is encouraged to telephone Applicants' undersigned attorney at the number noted below so that same can be resolved without the necessity of an additional action and response thereto.

Allowance of the application is awaited.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: _____
Leonard C. Mitchard
Reg. No. 29,009

1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100
Attachments: Peeples declaration; power of attorney

**APPENDIX**

Marked up version of clams under 37 CFR 1.121(c)

320 (Amended). A method as in claim 318 [or 319] wherein said Newcastle disease virus is strain MK107.

322 (Amended). A method as in claim 318 [or 319] wherein said virus is administered by the intravenous route.

328 (Amended). A method as in claim 318 [327] wherein said virus is administered by the intravenous route.